Clinical trial results:
Paricalcitol Trial: Phase II, Open label clinical trial of Paricalcitol in combination with Gemcitabine/ Nab-Paclitaxel therapy in advanced pancreatic cancer.

Summary

EudraCT number	2020-000073-24
Trial protocol	IE
Global end of trial date	30 September 2022

Results information

Result version number	v1 (current)
This version publication date	03 November 2023
First version publication date	03 November 2023

Trial information

Trial identification

Sponsor protocol code	CTRIAL-IE-19-33

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Cancer Trials Ireland
Sponsor organisation address	RCSI House, Dublin, Ireland, D02 H903
Public contact	Clinical Project Manager, Cancer Trials Ireland, +353 16677211 , info@cancertrials.ie
Scientific contact	Clinical Project Manager, Cancer Trials Ireland, +353 16677211 , info@cancertrials.ie

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	21 August 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 September 2022
Global end of trial reached?	Yes
Global end of trial date	30 September 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the anti-tumour efficacy of paricalcitol in combination with gemcitabine and nab-paclitaxel in patients with advanced pancreatic cancer who have received no prior systemic chemotherapy in the metastatic or recurrent setting.

Protection of trial subjects:

This clinical study was designed, implemented, and reported in accordance with the International Conference on Harmonization (ICH) Harmonized Tripartite Guidelines for Good Clinical Practice (GCP) and all applicable local regulations. The study was approved by the HPRA and Cork Teaching Hospitals Clinical Research Ethics Committee.

Background therapy:

N/A

Evidence for comparator:

The purpose of this study is to evaluate the effectiveness and safety of the combination of paricalcitol in combination with gemcitabine and nab-paclitaxel in patients with advanced pancreatic cancer who have received no prior systemic chemotherapy in the metastatic or recurrent setting.

Actual start date of recruitment	01 April 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Ireland: 15
Worldwide total number of subjects	15
EEA total number of subjects	15

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0

Adolescents (12-17 years)	0
Adults (18-64 years)	4
From 65 to 84 years	11
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

15 patients were consented over 5 sites from 28 Oct 2020 to 20 Oct 2021. All patients who provided informed consent, were registered to the study and provided demographic and/or baseline screening assessments.

Pre-assignment

Screening details:

The target population is patients with incurable recurrent, locally advanced metastatic pancreatic adenocarcinoma based upon biopsy-proven disease and radiological imaging, based on RECIST v1.1 criteria. All patients must fulfil all inclusion criteria and none of the exclusion criteria.

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Overall Trial

Arm description:

GEM (1,000 mg/m2) and Nab-paclitaxel (125 mg/m2 of BSA), on days 1, 8, 15 of each 28-day cycle PLUS Paricalcitol, 12mcg once daily, orally every day of the 28-day cycle

Arm type	Experimental
Investigational medicinal product name	Paricalcitol
Investigational medicinal product code	PR1
Other name	Zemplar
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

12mcg once daily, orally every day of the 28-day cycle.

Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	PR2
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1,000 mg/m2 on days 1, 8, 15 of each 28-day cycle. Dosing calculated as per Body Surface Area.

Investigational medicinal product name	nab-Paclitaxel
Investigational medicinal product code	PR3
Other name	Abraxane
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

125 mg/m2 on days 1, 8, 15 of each 28-day cycle. Dosing calculated as per Body Surface Area.

Number of subjects in period 1	Overall Trial
Started	15
Completed	0
Not completed	15
Physician decision	3
Trial Closure	1
Death	2
Clinical Disease Progression	2
Unacceptable Toxicity	3
Radiological Disease Progression	4

Baseline characteristics

Reporting groups	
Reporting group title	Overall Trial
Reporting group description:	
Fifteen patients were registered and received study treatment.	

Reporting group values	Overall Trial	Total	
Number of subjects	15	15	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	4	4	
From 65-84 years	11	11	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	66.9		
standard deviation	± 10.74	-	
Gender categorical Units: Subjects			
Female	7	7	
Male	8	8	
Race Units: Subjects			
Caucasian	14	14	
Black	1	1	
Staging Units: Subjects			
Locally advanced inoperable	3	3	
Metastatic	12	12	
Tumour Grade Units: Subjects			
Grade I	1	1	
Grade II	3	3	
Not Available	11	11	
Height Units: centimetre			
arithmetic mean	165.6		
standard deviation	± 8.95	-	
Height Units: centimetre			

median	168		
full range (min-max)	151 to 179	-	
Weight Units: kilogram(s)			
arithmetic mean	71.43		
standard deviation	± 15.642	-	
Weight Units: kilogram(s)			
median	71.30		
full range (min-max)	39.7 to 100.4	-	
Body Surface Area at Baseline Units: square metre			
arithmetic mean	1.786		
standard deviation	± 0.2233	-	
Body Surface Area at Baseline Units: square metre			
median	1.820		
full range (min-max)	1.30 to 2.13	-	

End points

End points reporting groups

Reporting group title	Overall Trial

Reporting group description:

GEM (1,000 mg/m2) and Nab-paclitaxel (125 mg/m2 of BSA), on days 1, 8, 15 of each 28-day cycle PLUS Paricalcitol, 12mcg once daily, orally every day of the 28-day cycle

Primary: Progression-free Survival (PFS)

End point title	Progression-free Survival (PFS)[1]

End point description:

Anti-tumour efficacy of treatment with paricalcitol will be primarily measured as progression free survival (PFS): that is, the percentage of patients free of progression at 24 weeks from registration into the study as determined by radiographic disease assessments per RECIST v1.1.
One patient who died due to an AE is included in the PFS analysis.
Two patients who did not have any post-baseline RECIST assessments but died on-study for reasons of clinical disease progression are included in the PFS analysis as having progressed.
Two patients who were withdrawn before post-baseline RECIST assessments were performed and had no evidence of clinical progression are excluded from the PFS analysis.

End point type	Primary

End point timeframe:

Time from registration to disease progression or death from any cause, censored at date last known to be progression-free for those who have not progressed or died. The primary outcome is PFS at 24 weeks.

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: This is a single arm study with no comparison groups therefore statistical analyses (comparison analysis) were not conducted.

End point values	Overall Trial			
Subject group type	Reporting group			
Number of subjects analysed	13[2]			
Units: Weeks				
median (confidence interval 95%)				
Median Time to Event (weeks)	14.57 (7.86 to 24.00)			
Estimated PFS Rate at 24 weeks	17.95 (2.92 to 43.38)			

Notes:

[2] - 2 Patients had no post-baseline assessments of disease and were not evaluable for the PFS analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

End point title	Overall Survival

End point description:

Twelve of the fifteen patients (80%) died on-study.

End point type	Secondary

End point timeframe:

Overall Survival at 24 weeks

End point values	Overall Trial			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: Weeks				
median (confidence interval 95%)				
Median Time to Event (Weeks)	24.14 (14.57 to 42.43)			
Estimated OS Rate at 24 weeks	51.33 (21.80 to 74.68)			

Statistical analyses

No statistical analyses for this end point

Secondary: Confirmed Tumour Response Rate

End point title	Confirmed Tumour Response Rate

End point description:

The analysis of tumour response rate was not performed as only 1 patient (8.3%) met the criteria for confirmed response with a partial response.
Three patients who did not have any post-baseline RECIST assessment or any evidence of progression are excluded from the analysis.
Two patients who did not have any post-baseline RECIST assessment but whose cause of death was disease progression are included in the analysis

End point type	Secondary

End point timeframe:

Tumour response rate at 24 weeks

End point values	Overall Trial			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Number of Patients				
Partial Response	1			
Stable Disease	5			
Progressive Dsease	6			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Treatment Failure (TTF)

End point title	Time to Treatment Failure (TTF)

End point description:

Fourteen patients were included in the analysis of treatment failure. 1 patient who had no post-baseline RECIST assessments and no evidence of clinical progression and had not discontinued study treatment (on treatment for 4 weeks) at the time of study closure is excluded from the TTF analysis. One patient who had no post-baseline RECIST assessments and no evidence of clinical progression is included in the analysis due to discontinuation of study treatment for an AE.

End point type	Secondary

End point timeframe:

Time from registration to discontinuation of therapy or ad-on of new anti-cancer therapy for any reason (including death, progression and toxicity).

End point values	Overall Trial			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: Weeks				
median (confidence interval 95%)				
Median Time to Event (weeks)	12.29 (6.14 to 24.14)			
Estimated TRF Rate at 24 weeks	28.57 (8.83 to 52.37)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Only treatment-emergent AEs (TEAEs), AEs beginning on or after the start date of study drug administration and up to 30 days after last administration.

Adverse event reporting additional description:

Adverse events (AEs) were coded using the Medical Dictionary for Regulatory Activities (MedDRA) central coding dictionary, version 25.1.
If a patient experienced more than one TEAE within a PT, only the TEAE with the highest grade/relationship was included in the summaries.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	Overall Trial

Reporting group description:

GEM (1,000 mg/m2) and Nab-paclitaxel (125 mg/m2 of BSA), on days 1, 8, 15 of each 28-day cycle PLUS Paricalcitol, 12mcg once daily, orally every day of the 28-day cycle

Serious adverse events	Overall Trial		
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 15 (86.67%)		
number of deaths (all causes)	12		
number of deaths resulting from adverse events	2		
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Thrombotic microangiopathy			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Superficial vein thrombosis			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			

Atrial fibrillation				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Dysarthria				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Facial paresis				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Malaise				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	2 / 15 (13.33%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Oedema peripheral				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Fatigue				
subjects affected / exposed	2 / 15 (13.33%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
General physical health deterioration				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			

Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Abdominal pain			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Infection	Additional description: Infection of unknown source		

subjects affected / exposed	1 / 15 (6.67%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Rash pustular				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Abdominal infection				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Bacterial infection				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Soft tissue infection				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Product issues				
Device leakage				

subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hypercalcaemia			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Overall Trial		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 15 (100.00%)		
Vascular disorders			
Hypotension			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		
Superficial vein thrombosis			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Embolism			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Peripheral venous disease			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	14 / 15 (93.33%)		
occurrences (all)	37		
Non-cardiac chest pain			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		
Pyrexia			

subjects affected / exposed	5 / 15 (33.33%)		
occurrences (all)	5		
Oedema peripheral			
subjects affected / exposed	5 / 15 (33.33%)		
occurrences (all)	6		
Chills			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Pain			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	3		
Implant site bruising			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Implant site pain			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Generalised oedema			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Discomfort			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Asthenia			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		
Malaise			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			

Dysphonia	Additional description: Hoarseness		
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Epistaxis			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Dyspnoea			
subjects affected / exposed	8 / 15 (53.33%)		
occurrences (all)	11		
Pulmonary embolism			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		
Pleuritic pain			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		
Pleural effusion			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Cough			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	2		
Vocal cord cyst			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Hypoxia			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Pulmonary oedema			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Hiccups			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	2		
Psychiatric disorders			
Confusional state			

subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		
Insomnia			
subjects affected / exposed	4 / 15 (26.67%)		
occurrences (all)	5		
Hallucination			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Depression			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Agitation			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Delirium			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Poor quality sleep			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Anxiety			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	2		
Depressed mood			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		
Investigations			
Platelet count decreased			
subjects affected / exposed	4 / 15 (26.67%)		
occurrences (all)	17		
Blood bilirubin increased			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	2		
Blood alkaline phosphatase increased			
subjects affected / exposed	3 / 15 (20.00%)		
occurrences (all)	7		

Aspartate aminotransferase increased				
subjects affected / exposed	3 / 15 (20.00%)			
occurrences (all)	12			
Gamma-glutamyltransferase increased				
subjects affected / exposed	2 / 15 (13.33%)			
occurrences (all)	3			
Alanine aminotransferase increased				
subjects affected / exposed	2 / 15 (13.33%)			
occurrences (all)	10			
Mean cell haemoglobin increased				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences (all)	1			
Mean cell haemoglobin concentration increased				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences (all)	1			
Blood chloride decreased				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences (all)	1			
Blood albumin decreased				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences (all)	1			
Blood lactate dehydrogenase increased				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences (all)	1			
Vitamin B2 increased				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences (all)	1			
Red blood cell count decreased				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences (all)	1			
Mean cell volume increased				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences (all)	1			
Lymphocyte count decreased				

subjects affected / exposed occurrences (all) Monocyte count decreased subjects affected / exposed occurrences (all) Blood urea increased subjects affected / exposed occurrences (all) Carbon dioxide decreased subjects affected / exposed occurrences (all) Creatinine renal clearance decreased subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1 1 / 15 (6.67%) 1 2 / 15 (13.33%) 2 1 / 15 (6.67%) 1 1 / 15 (6.67%) 3		
Injury, poisoning and procedural complications Fall subjects affected / exposed occurrences (all) Contusion subjects affected / exposed occurrences (all) Infusion related reaction subjects affected / exposed occurrences (all)	2 / 15 (13.33%) 4 2 / 15 (13.33%) 3 1 / 15 (6.67%) 1		
Cardiac disorders Atrial fibrillation subjects affected / exposed occurrences (all) Angina pectoris subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1 1 / 15 (6.67%) 1		
Nervous system disorders Peripheral sensory neuropathy subjects affected / exposed occurrences (all) Dizziness	3 / 15 (20.00%) 8		

subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		
Headache			
subjects affected / exposed	3 / 15 (20.00%)		
occurrences (all)	3		
Dyskinesia			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Migraine			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Neuropathy peripheral			
subjects affected / exposed	3 / 15 (20.00%)		
occurrences (all)	3		
Tremor			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Somnolence			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Facial paresis			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	7 / 15 (46.67%)		
occurrences (all)	24		
Thrombocytopenia			
subjects affected / exposed	5 / 15 (33.33%)		
occurrences (all)	7		
Neutrophil count decreased			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	3		
Neutropenia			
subjects affected / exposed	3 / 15 (20.00%)		
occurrences (all)	8		

Blood creatinine increased			
subjects affected / exposed	3 / 15 (20.00%)		
occurrences (all)	9		
White blood cell count decreased			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Pancytopenia			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	2		
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Eye disorders			
Eye disorder			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Visual field defect			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Vision blurred			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	2		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	6 / 15 (40.00%)		
occurrences (all)	15		
Diarrhoea			
subjects affected / exposed	8 / 15 (53.33%)		
occurrences (all)	14		
Vomiting			
subjects affected / exposed	8 / 15 (53.33%)		
occurrences (all)	14		
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Anal haemorrhage			

subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	7 / 15 (46.67%)		
occurrences (all)	14		
Abdominal pain upper			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		
Abdominal distension			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Abdominal pain			
subjects affected / exposed	5 / 15 (33.33%)		
occurrences (all)	8		
Mouth ulceration			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Dyspepsia			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Steatorrhoea			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Dry mouth			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Ascites			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Eructation			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Hepatobiliary disorders			
Jaundice			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		

Hepatomegaly				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences (all)	1			
Biliary obstruction				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences (all)	1			
Hyperbilirubinaemia				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences (all)	3			
Skin and subcutaneous tissue disorders				
Pruritus				
subjects affected / exposed	5 / 15 (33.33%)			
occurrences (all)	6			
Eczema				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences (all)	1			
Decubitus ulcer				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences (all)	1			
Skin ulcer				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences (all)	3			
Rash				
subjects affected / exposed	3 / 15 (20.00%)			
occurrences (all)	4			
Dermatitis acneiform				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences (all)	4			
Rash papular				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences (all)	1			
Rash erythematous				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences (all)	2			
Alopecia				

subjects affected / exposed occurrences (all) Rash maculo-papular subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1 1 / 15 (6.67%) 1		
Renal and urinary disorders Pollakiuria subjects affected / exposed occurrences (all) Acute kidney injury subjects affected / exposed occurrences (all) Renal failure subjects affected / exposed occurrences (all) Urinary incontinence subjects affected / exposed occurrences (all)	 1 / 15 (6.67%) 1 1 / 15 (6.67%) 2 1 / 15 (6.67%) 1 1 / 15 (6.67%) 1		
Endocrine disorders Hyperparathyroidism subjects affected / exposed occurrences (all)	 1 / 15 (6.67%) 1		
Musculoskeletal and connective tissue disorders Pain in extremity subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Muscular weakness subjects affected / exposed occurrences (all) Joint swelling subjects affected / exposed occurrences (all) Neck pain	 2 / 15 (13.33%) 4 4 / 15 (26.67%) 4 2 / 15 (13.33%) 2 1 / 15 (6.67%) 1		

subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		
Osteoporosis			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Infections and infestations			
COVID-19			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		
Rash pustular			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Skin infection			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Urinary tract infection			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		
Folliculitis			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		
Abdominal infection			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Cellulitis			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	3		
Soft tissue infection			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Sinusitis			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Infection			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		

Metabolism and nutrition disorders			
Hypercalcaemia			
subjects affected / exposed	11 / 15 (73.33%)		
occurrences (all)	40		
Hypophosphataemia			
subjects affected / exposed	3 / 15 (20.00%)		
occurrences (all)	4		
Hypokalaemia			
subjects affected / exposed	5 / 15 (33.33%)		
occurrences (all)	20		
Hyperglycaemia			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Decreased appetite			
subjects affected / exposed	7 / 15 (46.67%)		
occurrences (all)	9		
Weight decreased			
subjects affected / exposed	4 / 15 (26.67%)		
occurrences (all)	6		
Dehydration			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Hyponatraemia			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		
Hypoalbuminaemia			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	6		
Hypomagnesaemia			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Polydipsia			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Appetite disorder			

subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Hypocalcaemia			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 April 2021	Study protocol updated to Version 3 included updates to the study design section, patient eligibility, study treatment and assessments.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported